Hosp. Lib.

SECOND SERIES JANUARY 1940 VOL. 16, NO. 1

BULLETIN OF THE NEW YORK ACADEMY OF MEDICINE

CONTENTS

The Adrenal Medulla 3
W. B. Cannon

Hypothyroidism: Diagnosis and Treatment 14
J. H. Means

The Modern Treatment of Pyogenic Osteomyelitis . . 20
Dallas B. Phemister

Otitis Media and Its Extensions 24
Edmund Prince Fowler, Jr.

Obstetrics at the New York Almshouse and at Bellevue Hospital 38
Claude Edwin Heaton

Library Notes:

Recent Accessions 48

Deaths of Fellows 50

AUTHORS ALONE ARE RESPONSIBLE FOR OPINIONS EXPRESSED IN THEIR CONTRIBUTIONS

Published monthly by THE NEW YORK ACADEMY OF MEDICINE
2 East 103 Street, New York

Entered as second-class matter, February 3, 1928, at the Post Office at New York, N. Y., under the Act of August 24, 1912. Subscription, United States, Canada and Cuba, $3.00; all other countries, $4.00 a year. Single copies, 50c.

OFFICERS AND STAFF OF THE ACADEMY

1940

President

MALCOLM GOODRIDGE

Vice-Presidents

BENJAMIN P. WATSON
RUFUS I. COLE
I. OGDEN WOODRUFF

Treasurer

BERNARD SACHS

Assistant Treasurer

RODERICK V. GRACE

Recording Secretary

JAMES RALPH SCOTT

Trustees

CARY G. BURDICK
CARL EGGERS
*MALCOLM GOODRIDGE
JOHN A. HARTWELL
SHEPARD KRECH
JAMES ALEXANDER MILLER
WALTER L. NILES
WALTER W. PALMER
EUGENE H. POOL
*BERNARD SACHS
*JAMES RALPH SCOTT
FREDERIC E. SONDERN
CHARLES F. TENNEY

Council

The President — The Vice-Presidents — The Trustees
The Treasurer — The Recording Secretary
The Chairmen of Standing Committees

Director

HERBERT B. WILCOX

Librarian

ARCHIBALD MALLOCH

Executive Secretary
Public Health Relations Committee
E. H. L. CORWIN

Executive Secretary
Committee on Medical Education
MAHLON ASHFORD

Executive Secretary, Committee on Medical Information

IAGO GALDSTON

Library Consultants

LAURA E. SMITH
B. W. WEINBERGER
ARNOLD C. KLEBS

Legal Counsel

FRANK L. POLK, ESQ.

EDITORIAL BOARD

JEROME P. WEBSTER, *Chairman*
ALFRED E. COHN
EUGENE F. DUBOIS
ROBERT F. LOEB
ARCHIBALD MALLOCH
PHILIP VAN INGEN
KARL VOGEL
MAHLON ASHFORD, *Editor*

* Ex-officio

BULLETIN OF
THE NEW YORK ACADEMY
OF MEDICINE

JANUARY 1940

THE ADRENAL MEDULLA*

W. B. CANNON

Professor of Physiology, Harvard University

A FACT of fundamental importance in understanding the functioning of the adrenal medulla is its embryonic origin. Neuroblasts migrating outward from the primitive axis of spinal cord segments develop mainly into the ganglia of the sympathetic system; but some of them are transformed into the adrenal medulla. Thus most of these neuroblasts become sympathetic neurones; a small remnant become secreting cells which, on being stimulated, discharge adrenaline. Likewise, nearly all sympathetic neurones, when they are stimulated, discharge at their endings a substance which, according to strong presumptive evidence, has been regarded as adrenaline (Rosenblueth[1], 1932). Since adrenaline is the characteristic constituent when extracts are made of the adrenal medullary cells and since sympathetic neurones are like the medullary cells in origin and in producing adrenaline, or an adrenaline-like substance, the question arose whether extracts of these neurones might not yield adrenaline.

The answer to that question was sought by Lissák and myself[2]

* Presented October 27, 1939 at The New York Academy of Medicine in the Twelfth Graduate Fortnight.

NYK

(1939). We found that extracts of the ultimate sympathetic fibers, the "adrenergic" fibers (e.g., those in the mesenteric nerves) or extracts of an organ containing such fibers (e.g., the heart) have all the effects of extracts of the adrenal medulla itself. They are like adrenaline in raising blood pressure, dilating the pupil, contracting the nictitating membrane, relaxing the non-pregnant cat uterus, augmenting the heart beat, and in other similar respects. Extracts of "cholinergic" nerves, and also extracts of the heart in which adrenergic fibers had degenerated, had no distinctive adrenaline-like action on blood pressure or iris.

The evidence strongly indicates, therefore, that Elliott's[3] (1904) suggestion is correct, that the ultimate sympathetic neurones influence glands and cardiac and smooth muscle by the adrenaline which they set free at their terminals, and that adrenaline secreted from the adrenal medulla and circulating in the blood stream has on these structures the same influence as the nerve impulses because it is the same substance as that which they produce. Since the sympathetic division of the autonomic system when strongly excited acts as a whole and thereby induces wide-spread changes in the organism—e.g., stopping the digestive processes, raising blood pressure, accelerating the heart, erecting hairs, as well as discharging adrenaline from the adrenal medulla—the combined, simultaneous action of sympathetic neuronal adrenaline and secreted medullary adrenaline is properly regarded as constituting a sympathico-adrenal system.

In addition to adrenaline discharged from the adrenal medulla, as a means of reinforcing or prolonging the effects of sympathetic nerve impulses, there is sympathin. This is a substance which escapes into the blood stream, from organs innervated by the sympathetic, when the sympathetic system is specially active. As we have noted, in these circumstances adrenaline is discharged from the nerve endings and has its typical effects. In doing so, however, some change occurs, because in some regions—in smooth muscles, for example—it causes relaxation and in others contraction. Rosenblueth and I[4] (1933), following a theory offered by Langley, have suggested that neuronal adrenaline unites inside the reacting cells with a differentiating substance which makes possible the two opposite responses to a single agent. In any case, sympathin differs from adrenaline. For example, ergotoxine blocks the hypertensive action of adrenaline on blood pressure and reveals a depressive action; it has not that influence on the action of sympathin.

And whereas adrenaline retracts the iris and relaxes the cat's non-pregnant uterus, sympathin does not do so if it comes from a region where sympathetic nerves have a purely positive influence. In general, however, the positively acting sympathin prevails, causing, for example, acceleration of the heart and rise of blood pressure. The observations which Rosenblueth and I[5] made in 1932, and which later were extended by Liu[6] (1935), proved that secreted adrenaline and circulating sympathin, liberated from stimulated structures, coöperate in augmenting or lengthening the duration of such changes. A brief period of excitement will discharge adrenaline from sympathetic nerve endings; sympathin will come away from the affected organs and also adrenaline from the adrenal medulla. These circulating sympathico-mimetic substances may have effects which outlast for minutes the exciting incident—effects which possibly explain the agitation which is experienced after the object or condition, which produced the excitement originally, has disappeared.

There was a time, about twenty years ago, when a lively controversy was going on between Stewart and Rogoff, then of Cleveland, and a group in the Harvard Physiological Laboratory as to whether the adrenal medulla responds to changes involving the sympathetic system by an extra discharge of adrenaline (Cannon,[7] 1929). The Cleveland investigators themselves furnished evidence that adrenal secretion is under control of the splanchnic nerves, for when they stimulated these nerves they saw a retraction of the denervated iris—a retraction which did not occur if the blood flow through the adrenal veins was obstructed during the stimulation, and which did occur when the pent blood was released. They denied the claims of the Harvard group, however, that afferent stimulation and asphyxia, which are accompanied by a natural discharge of splanchnic impulses, induce a similar increase of the secretion. In 1922, Carrasco-Formiguera and I,[8] using as an indicator the denervated heart instead of the denervated iris, provoked an acceleration of the heart rate by stimulating afferent nerves or inducing asphyxia. When we obstructed the blood flow through the adrenal veins these reflex and asphyxial effects did not occur, and when the pent blood was released the heart was again accelerated. The logic of the situation thus presented required Stewart and Rogoff to accept our evidence for reflex and asphyxial secretion from the adrenal medulla or to repudiate the evidence on which they based the conclusion that the output of

adrenaline is under splanchnic control. That dilemma has not been met in the past seventeen years.

In reports of the work done by Stewart and himself, Rogoff[9] (1935) has repeatedly and insistently laid stress on the fact that they employed a quantitative method. The method involved collecting blood from the adrenal veins as it gathered during a measured time in a section of the inferior vena cava, the so-called "cava pocket," and then assaying the adrenaline content of this blood by comparing its effect and that of various concentrations of adrenaline on a beating intestinal strip. By use of this method the Cleveland investigators obtained results which led them to infer that adrenal secretion is constant and unvarying; indeed, Rogoff has declared that the conclusion that asphyxia and central stimulation induce an extra output of adrenaline "has never been supported by satisfactory measurements of the rate of secretion." That statement indicates disregard for the results obtained by Rapport and myself[10] (1921), and by Sataké and his colleagues[11] (1927) with use of the very method which Stewart and Rogoff devised. For more than a dozen years the Japanese investigators labored in this field. They published a large volume of experimental studies which definitely and quantitatively confirmed the results obtained by the Harvard group and which also clearly explained Stewart-and-Rogoff's failure as being due to too deep anesthesia. Rogoff has not only not attended to this evidence contradictory to his views; he has not attended to the studies of various observers—in Europe, Africa, South America—who with different methods have supported consistently our conclusions. Indeed, in the past twenty years there has been no support whatever, from any quarter, for the claims of the Cleveland pair. I offer no apology for recalling this old controversy, because there still appear in text books and even in a fairly recent publication of the American Medical Association (Rogoff,[9] 1935) statements which lead readers to conclude that the issue is not fully settled and that there is still some question about extra adrenal secretion when the sympathetic system is active.

As I have intimated, in the course of this controversy the denervated heart was used as an indicator of increased adrenaline in the circulation. It is extremely sensitive, responding by a faster beat when the adrenaline concentration is increased by only 1 part in 1,400,000,000 parts of blood. When, with aseptic precautions, the heart has been isolated from the nervous system the animal may live indefinitely, with the heart con-

tinuing to perform its proper functions as a pump (Cannon, Lewis and Britton,[12] 1926). Hence, while the animal is in excellent physical condition, records can be made of the heart rate under various experimental conditions and thereafter the adrenal glands can be excluded from action—by removing one of them and denervating the other—and records of the heart rate then made again under the same conditions. Thus, by finding that an acceleration occurred during the tests, and that acceleration failed to occur after adrenal inactivation, we were able to show that muscular work, emotional excitement, asphyxia, low blood pressure, external cold, infection, and hypoglycemia were accompanied by an extra secretion from the adrenal medulla, and extra activity of the sympathico-adrenal system.[9,10,11,12] Each one of these situations makes a special demand on the organism or is likely to make that demand. In each one of them the operation of the system is such as to favor the welfare of the organism. The blood flow is shifted in such manner as to promote effectiveness in muscular effort, the metabolic rate is speeded up when the temperature tends to fall, glucose is liberated from hepatic stores when the amount in the blood is dropping to a low level, the capacity of the blood vessels is adapted to a reduced blood volume. In short, as these illustrations indicate, the system promptly and automatically makes adjustments which are required to prepare the organism for temporary exigencies or to preserve its normal internal condition when that is likely to be disturbed. Such services performed by the sympathico-adrenal system at times of unusual or critical need I have called its "emergency" functions (Cannon,[7] 1929).

Much of the evidence that the sympathico-adrenal system performs its special services in times of stress was gained by study of animals—dogs, cats, monkeys—from which that system had been wholly removed. The possibility of continued existence without any sympathetic nerves may seem surprising, for they belong to what have been called "Lebensnerven." Yet we have been able, quite easily, to keep sympathectomized animals under the quiet and uniform conditions of the laboratory many months—in one instance more than three years—in good health and nutritional status. Cats were most thoroughly investigated. So long as they were not subjected to stress they appeared quite normal. But when they were exposed to heat or cold they were revealed as defective in their ability to maintain body temperature; when they lost blood they were defective in restoring compensatory blood pressure; when they

ran or struggled the blood pressure fell and they fainted; when placed in an atmosphere of low oxygen concentration they collapsed much sooner than animals with the sympathico-adrenal system intact; and when given insulin in amounts readily endured by normal cats they suffered a sharp drop in blood-sugar percentage which would have been disastrous if they had not been rescued (Cannon,[13] 1939). It was interesting to learn that although sympathectomized dogs showed in emergencies effects similar to those shown by sympathectomized cats the effects were not so extreme. The difference can reasonably be ascribed to the remarkable physiological developments which the dog possesses as a running animal: a much larger lung surface, cardiac capacity and blood volume for his weight than the more indolent cat possesses, in addition to having a higher hemoglobin percentage, a readier resort to shivering when cold and resort to panting when warm. Note that in all these respects removal of the sympathico-adrenal system produces no adverse alteration. There is one condition in which these advantages of the dog cannot be effective—i.e., in the mobilization of sugar from the liver when an excess of insulin is given. In those circumstances the sympathectomized dog is as vulnerable as the sympathectomized cat (Cannon,[14] 1939). It appears, therefore, that the sympathico-adrenal system is called into action in emergencies and has a fundamentally important function in maintaining a fairly uniform condition in the fluid matrix of the organism, the blood and lymph (Cannon,[13] 1939).

The foregoing discussion has been concerned chiefly with the combined functions of the sympathetic division of the autonomic system and the secretion of the adrenal medulla—i.e., with the functions of the sympathico-adrenal system. The question arises as to whether secreted adrenaline, itself, has a distinctive use. Rogoff[9] (1935) has declared that it does not play an important role in the body and that "no specific function for epinephrine (adrenaline) has been proved." The main argument against the utility of secreted adrenaline is based on the fact that one adrenal may be removed and the other may be demedullated without endangering the life of the animal. Obviously the adrenal medulla is not essential to existence. There is a difference, however, between being useful and being essential. As we have many times demonstrated, the cardiac nerves may all be severed in animals which survive the operation for many months; the nerves are clearly not essential, but is there anyone who would suppose, therefore, that they are not useful? Simi-

larly the survival of animals without the sympathetic system proves that it is not essential, but again are we to conclude, therefore, that it is not useful? In order to know the utility of adrenaline we must consider what changes are wrought by exclusion of the adrenal medulla, quite apart from continued existence.

First, there is the coöperation between secreted adrenaline, neuronal adrenaline and circulating sympathin, already referred to. Actual records show, as previously noted, that a momentary excitement may have bodily effects lasting 15 to 20 minutes if the adrenals are present and only brief effects if the glands are excluded from action. These records prove that adrenaline intensifies and prolongs the influence of sympathetic impulses.

Again, adrenaline has an accelerating action on metabolism. One milligram of adrenaline will cause an increased output of heat amounting to 50 calories. I have already mentioned the evidence, derived from experiments on animals with the heart denervated, that when the body temperature tends to drop, because of exposure to external cold, there is an increased secretion from the adrenal medulla. If the adrenal influence is suppressed and the animals, thus rendered defective, are subjected to the same conditions as before, shivering occurs to a greater degree than when the adrenals were present and able to augment metabolism, i.e., the animals fall back on muscular contraction as a means of producing extra heat.

Another effect of adrenaline which has been reported by a number of investigators—among them Mendenhall and myself[15] (1914)—is that of hastening the coagulation of the blood. When adrenaline is injected this phenomenon occurs, and when adrenaline is secreted, either as a consequence of splanchnic stimulation or as a consequence of excitement, the time of coagulation is likewise greatly shortened. If the adrenal medulla is excluded and the conditions which normally evoke secretion are repeated, the faster clotting does not occur.

Finally, there is the special effect of adrenaline on the liver. In 1928 Riegele[16] described a network of extremely delicate nerve filaments between the liver cells, with offshoots reaching into the cellular cytoplasm. This observation, if correct, would establish a basis for immediate nervous government of liver function. The observation, however, has been questioned. Two years ago Nonidez[17] (1937) reported that the silver method used by Riegele not only may stain nerve fibers but

also may impregnate fine connective tissue strands and thus confuse the picture. "Up to the present," Nonidez wrote, "no nervous structure resembling a network has been described in the liver."

The testimony that nerve filaments are not distributed to liver cells is in accord with the evidence that a relatively small dose of insulin induces a swift and unchecked and quite abnormal fall of blood sugar in animals from which the adrenals have been removed, although hepatic nerves are still intact (Cannon, McIver and Bliss,[18] 1924). It is also in accord with observations that emotional excitement does not cause the usual hyperglycemia in animals without adrenals, but again with hepatic nerves intact (Britton,[19] 1928). Supporting evidence was furnished by the experiments which Lissák and I[2] (1939) performed this year. It will be recalled that we found an adrenaline-like substance in the ultimate sympathetic neurones, whether these neurones, or parts of them, were isolated or were imbedded in organs, e.g., the heart. The significant fact appeared, that whereas extracts of liver *blood vessels* raised blood pressure, dilated the pupil and speeded up the heart rate—thereby revealing the presence of sympathetic fibers on them—extracts of liver *pulp* had little or no adrenaline-like action. The occasional slight action can be explained as due to the difficulty of removing the pulp from the vessels without pulling away some of the vascular twigs. All these observations, taken together, indicate clearly that the liver cells are not subject to direct nervous control.

It appears that the liver can play a role in carbohydrate metabolism quite independently, both by taking in and giving forth glucose. By a simultaneous determination of the rate of blood flow through the liver and the glucose content of the inflowing and the outflowing blood it has been shown that during control periods the liver secretes glucose, and that when glucose is abundantly supplied secretion ceases and sugar is retained (Soskin, Essex, Herrick and Mann,[20] 1938). In an emergency, however, as, for example, in great excitement or when insulin is abundant, this intrinsic mechanism is not adequate. Faster glycogenolysis is required in order to mobilize blood sugar. In these circumstances, adrenaline discharged from the adrenal medulla is the effective agent for releasing glucose from the hepatic stores.

Because an injection of adrenaline raises blood pressure, by accelerating the heart and constricting arterioles, an idea has prevailed that persistent hypertension may result from overactivity of the adrenal

medulla. In a temporary test, as Freeman and Jeffers[21] (1939) have shown, secreted adrenaline may play a significant role in producing a brief experimental hypertension, but that occurred when the heart was denervated and when its acceleration depended on medulliadrenal secretion. If the heart was normally innervated, the effect was produced quite as well without any participation of the adrenal glands. Again we note a coöperation of adrenaline and sympathetic impulses in the sympathico-adrenal system—a coöperation which permits either of the partners to compensate, in this condition, for absence of the other. But neither of these partners is necessary for the maintenance of normal blood pressure. The entire sympathetic system may be progressively removed and yet vascular tone is well preserved and the pressure is held within the normal range (B. Cannon,[22] 1931). This is not a consequence of compensatory secretion of adrenaline, for there is experimental proof that the adrenal medulla does not secrete unless it is stimulated by nervous impulses, except in the rare state of extreme asphyxia (Zwemer and Newton,[23] 1928). The sustained contraction of the arterioles after sympathectomy appears to be due to intrinsic properties of the smooth muscle in the vessel walls.

Two types of prolonged hypertension can be produced experimentally: one the result of removal of the restraining nerves (i.e., those from the carotid sinus and the aortic arch), as demonstrated by Heymans and his collaborators; the other the result of lessening the blood flow through the kidneys, as demonstrated by Goldblatt and his collaborators (Cannon,[24] 1937). The former type, Heymans and Bouckaert[25] (1936) report, disappears when the sympathico-adrenal system is entirely excluded from action. Whether this type ever occurs clinically is as yet unknown. The second type—that produced by Goldblatt clips on the renal arteries—is not affected by sympathectomy. Freeman and Page[26] (1937) have found that application of the clips induced hypertension in completely sympathectomized animals and that if hypertension had been produced by partial renal ischemia, later removal of the sympathetic did not improve the condition. I have felt justified in emphasizing the absence of evidence that excessive adrenal secretion explains high blood pressure because, unfortunately, the idea that the adrenals are the cause of it has prevailed and has led to severe operations directed towards denervating them in order to abolish their supposedly pernicious discharge. There is no doubt that if adrenal secre-

tion should be discharged in sufficient amount to produce a high blood pressure it would have other wide-spread and highly disturbing effects on the organism such as are, in fact, not seen in cases of hypertension.

In summarizing the part played by the adrenal medulla in the functioning of the organism we may recognize that it coöperates with sympathetic impulses in producing adrenaline, that this sympathico-adrenal system is brought prominently and usefully into action in emotional excitement, in vigorous muscular work, in asphyxia, low blood pressure, chilling surroundings and hypoglycemia—in brief, that it serves effectively in emergencies; furthermore, that this service can be given a general expression in stating that the system guards the constancy of the internal environment of the organism; and finally that secreted adrenaline itself acts to prolong the effects of nerve impulses, to accelerate metabolism, to shorten coagulation time and to release glucose from the liver. There is no evidence that secreted adrenaline is an important agent in maintaining a high blood pressure.

REFERENCES

1. Rosenblueth, A. The chemical mediation of autonomic nervous impulses as evidenced by summation of responses, *Am. J. Physiol.*, 1932, *102:* 12.
2. Cannon, W. B. and Lissák, K. Evidence for adrenaline in adrenergic neurones, *Am. J. Physiol.*, 1939, *125:* 765.
3. Elliott, T. R. On the action of adrenalin, *J. Physiol.*, 1904, *31:* xx.
4. Cannon, W. B. and Rosenblueth, A. Sympathin E and sympathin I, *Am. J. Physiol.*, 1933, *104:* 557.
5. Rosenblueth, A. and Cannon, W. B. Some effects of sympathin on the nictitating membrane, *Am. J. Physiol.*, 1932, *99:* 398.
6. Liu, A. C. The coöperative action of sympathetic nerve impulses, adrenine and sympathin on the nictitating membrane of the cat, *Am. J. Physiol.*, 1935, *112:* 690.
7. Cannon, W. B. *Bodily changes in pain, hunger, fear and rage.* New York, Appleton, 2. ed., 1929.
8. Cannon, W. B. and Carrasco-Formiguera, R. Further evidence for reflex and asphyxial secretion of adrenin, *Am. J. Physiol.*, 1922, *61:* 215.
9. Rogoff, J. M. The adrenal medulla, in: *Glandular physiology and therapy.* Chicago, A.M.A., 1935, p. 279.
10. Cannon, W. B. and Rapport, D. Further observations on the denervated heart in relation to adrenal secretion, *Am. J. Physiol.*, 1921-22, *58:* 308.
11. Sataké, Y., Sugawara, T. and Watanabé, M. Method for collecting blood from suprarenal gland in the dog, *Tohoku J. Exper. Med.*, 1927, *8:* 501; and Effect of fastening and of sensory stimulation upon the rate of epinephrine output from the suprarenal gland in dogs, *ibid.*, 1927, *9:* 1.
12. Cannon, W. B., Lewis, J. T. and Britton, S. W. Lasting preparation of the denervated heart for detecting internal secretion with evidence for accessory accelerator fibers from the thoracic sympathetic chain, *Am. J. Physiol.*, 1926, *77:* 326.
13. Cannon, W. B. *The wisdom of the body.* New York, Norton, Rev. ed., 1939.
14. Cannon, W. B. Some new aspects of homeostasis (William Henry Welch lecture), *J. Mt. Sinai Hosp.*, 1939, *5:* 587.
15. Cannon, W. B. and Mendenhall, W. L.

The hastening of coagulation by stimulating the splanchnic nerves, *Am. J. Physiol.*, 1914, *34:* 243.

16. Riegele, L. Über das feinere Verhalten der Nerven in der Leber von Mensch und Säugetier, *Ztschr. f. mikr.-anat. Forsch.*, 1928, *14:* 73.
17. Nonidez, J. F. Nervous terminal reticulum. Critique; observations on the thyroid and the liver, *Anat. Anz.*, 1937, *84:* 1.
18. Cannon, W. B., McIver, M. A. and Bliss, S. W. A sympathetic and adrenal mechanism for mobilizing sugar in hypoglycemia, *Am. J. Physiol.*, 1924, *69:* 46.
19. Britton, S. W. The prepotency of medulliadrenal influence in emotional hyperglycemia, *Am. J. Physiol.*, 1928, *86:* 340.
20. Soskin, S., Essex, H. E., Herrick, J. F. and Mann, F. C. The mechanism of regulation of the blood sugar by the liver, *Am. J. Physiol.*, 1938, *124:* 558.
21. Freeman, N. E. and Jeffers, W. A. Effect of progressive sympathectomy on hypertension produced by increased intracranial pressure, *Am. J. Physiol.*, 1939, *126:* P493.
22. Cannon, B. The effects of progressive sympathectomy on blood pressure, *Am. J. Physiol.*, 1931, *97:* 592.
23. Zwemer, B. L. and Newton, H. F. Asphyxial stimulation of the denervated adrenal gland, *Am. J. Physiol.*, 1928, *85:* 507.
24. Cannon, W. B. Factors affecting vascular tone (George E. Brown memorial lecture), *Am. Heart J.*, 1937, *14:* 383.
25. Heymans, C. and Bouckaert, J. J. Hypertension artérielle chronique expérimentale et sympathectomie, *Bull. Acad. roy. de méd. de Belgique*, 1936, *1:* 42.
26. Freeman, N. E. and Page, I. Hypertension produced by constriction of renal artery in sympathectomized dogs, *Am. Heart J.*, 1937, *14:* 405.

HYPOTHYROIDISM
DIAGNOSIS AND TREATMENT*

J. H. MEANS

Jackson Professor of Clinical Medicine, Harvard University

THE term hypothyroidism obviously signifies a state in which the individual receives less of the hormone characteristic of the thyroid than is required by his body economy for the preservation of health. We are all quite familiar with such clinical varieties of hypothyroidism as cretinism, endemic or sporadic, and the myxedema of children and of adults. We also recognize hypothyroidism following extensive surgical removal of thyroid tissue, or destruction of thyroid tissue by certain types of chronic inflammation.

I have been asked to discuss with you the diagnosis and treatment of these conditions and that I will do: but I must say something also of etiology and morbid physiology because it is upon these that sound clinical practice must rest.

Adult myxedema was first described by Gull in 1874 and its cure by the administration of thyroid was contributed by Murray in 1891. It is of interest to note that Murray died September 23, last—the father of endocrine-substitution therapy. It is also worth noting that probably the first patient to receive his treatment in the United States is still alive at the age of eighty-seven. Mrs. B. is now the patient of Alexander Burgess, of Providence, who kindly gives me frequent bulletins of her progress. Her symptoms were first noted in 1888 and her doctor diagnosed Bright's disease and said she could not live six months. In 1892 another doctor, keener in diagnosis and up to date on his literature, diagnosed myxedema and started her on thyroid. She has taken it ever since.

The case of Mrs. B. teaches us the calamity of missing the diagnosis of myxedema. Had it not been made she would have died in 1903 or earlier, because fifteen years seems to be as long as one can live after the onset of myxedema without thyroid therapy. The symptoms and signs of myxedema are so striking, so characteristic, that there would seldom seem

* Delivered October 25, 1939 at The New York Academy of Medicine in the Twelfth Graduate Fortnight.

to be any excuse for missing the diagnosis. The classic picture should be familiar to every doctor, and if when present there can likewise be demonstrated low basal metabolic rate–minus thirty-five or lower–and elevated blood cholesterol, the diagnosis is practically certain. Nevertheless, in our clinic we get patients each year in whose cases the diagnosis has been missed. Often the error is in supposing that the patient has Bright's disease. Doctors thus give us the opportunity to make cures which they could easily have made themselves, and for which they could have got the credit.

A few years ago I would have told you that spontaneous, acquired myxedema of adults is due to primary atrophy of the thyroid; that the effect of this atrophy is to produce a simple athyreosis, the effects of which can be completely corrected by the administration of sufficient quantities of dried thyroid gland. The only reservation I would have made would have been that in patients with arteriosclerosis you must beware of producing angina pectoris by too rapid elevation of the rate of metabolism, with a resulting inadequacy of coronary blood flow.

Today these statements will still hold in most instances, but recent experience has indicated that there are a few cases of what clinically is myxedema in which the etiology is different and the indications for treatment different. These are cases in which the primary fault lies in the pituitary instead of in the thyroid. The myxedema is the result of a hypothyroidism due to lack of stimulation of the thyroid by the pituitary, rather than to primary failure of the thyroid itself. Actually these patients have a form of pituitary cachexia, or Simmonds' disease, but for reasons unknown, the emphasis in their symptomatology is so strikingly on their hypothyroid manifestations that other hypopituitary symptoms or signs escape attention in the clinical evaluation.

Our attention was drawn to this special type of myxedema by the following experience. A woman of forty-eight entered December 1, 1936, with what appeared to be fairly classic myxedema of about ten years' duration. On treatment with thyroid these manifestations disappeared. However, she soon developed new symptoms–nausea, vomiting, fever, psychosis and convulsions, and died on the thirtieth day of treatment. At autopsy there was found fibrosis of the anterior lobe of the pituitary and atrophy of the thyroid, parathyroids, adrenals, ovaries and uterus. These pathologic changes are characteristic of Simmonds' disease and the terminal symptoms are like those sometimes seen in the crises of

Addison's disease.[1]

More recently, my colleague, J. Lerman, referred to the hospital a woman of thirty years (U177833), whom he thought had ordinary myxedema. On thyroid therapy she also improved as to her myxedema manifestations, but presently went into an undoubted state of adrenal insufficiency, from which, however, she was rescued by vigorous treatment with sodium chloride.

Although rare, cases of this type are important, because of the hazards of treatment with thyroid. Their detection will depend upon the discovery of evidence of coexisting underfunction of other endocrine glands than the thyroid. In women developing myxedema prior to the menopause the occurrence of amenorrhea, in place of the usual menorrhagia of myxedema, would be very suggestive of the pituitary type. However, there may be no absolute method of recognition except by very careful control of thyroid therapy in all cases of myxedema; and to the well known danger of inducing angina pectoris, we may add the occasional one of producing Addisonian crisis.

The treatment of the usual type of myxedema is so simple that we need not devote much time to it. The objective should be to rid the patient of his symptoms and clinical signs with the smallest daily ration of thyroid by mouth that will accomplish this purpose. Usually this will be found to be in the neighborhood of one to one and a half grains of thyroid U. S. P., once daily. If such dosage produces any sort of untoward symptoms, angina or other, thyroid should be stopped for a few days and then resumed in smaller dosage. We have some patients who cannot tolerate rations of over one-half to three-quarters of a grain a day. During the inauguration of thyroid therapy the doctor, for the reasons given above, should have the patient under close surveillance; and only after the size of the permanent ration has been well established, is it wise to lengthen the time between check-ups.

The treatment of the pituitary type is far from simple. Persons so afflicted are in need of all the functions of the anterior lobe of the pituitary. This might be provided either by administering the anterior lobe hormones themselves; thyrotropic, adrenotropic, gonadotropic; or the hormones which the other endocrines make under anterior lobe stimulation, namely, thyroid, cortin, estrin.

As a matter of fact, in practice good results may probably be obtained in such cases by a combination of small doses of thyroid when the

patient is protected against adrenocortical insufficiency by a high salt intake, and some preparation containing the gonadotropic principles of the anterior lobe.

The effects of hypothyroidism are more serious when the state supervenes before growth has been attained than after. The adult who acquires myxedema, if normal before the disease began, can be made normal again by adequate treatment with thyroid. On the other hand, hypothyroidism during infancy or childhood, if long untreated, will result in physical and mental stunting which no amount of substitution therapy later can altogether alleviate. Indeed, cretinous children, who have reached ten years without treatment, derive little if any benefit from thyroid. About all the effect it has upon them is to make them irritable and less manageable than when in their athyreotic vegetable-like state. The earlier in life hypothyroidism occurs, and the longer the interval before adequate treatment is established, the more grave will be the consequence.

Thus the prognosis in cretinism, that is to say, congenital hypothyroidism, whether of the endemic or sporadic variety, is problematical. Certainly the outlook is brightest when the correct diagnosis is made very early in life and treatment started and maintained throughout the growth period and thereafter. Even so, on the question, whether an absolutely normal mental development can occur, authorities differ.

The early diagnosis of cretinism depends upon recognition of the significance of characteristic facies, habitus and behavior. It can be made in the early months of infancy. Among the earliest signs, as pointed out by Talbot,[2] are a heavy expression, and pig-like appearance of the eyes. A curious yellow tint appears early on the mesial aspect of the cheeks, disappearing when the infant cries. Changes in the tone of the voice in the direction of hoarseness are always important. Later the appearance of the cretin becomes thoroughly characteristic—a round stupid face, wide flat thick nose, open drooling mouth from which protrudes an over large tongue. The neck is short and thick, the trunk short, the belly prominent, always with umbilical hernia, the skin is dry and harsh, fat pads appear about the shoulders, and dentition is delayed.

Laboratory confirmation can be had by demonstration of low basal metabolic rate, elevated blood cholesterol, or by x-ray showing delayed bone age.

As soon as the diagnosis of cretinism is made, substitution therapy with thyroid should be started, and should be continued in adequate

dosage without interruption throughout life.

The criteria of adequate dosage are several. Not only have we basal metabolic rate and blood cholesterol as measuring sticks, but also bone age, height age, and mental age. I agree heartily with Wilkins,[3] who claims that it is not sufficient to maintain basal metabolic rate and cholesterol at normal levels, but that every effort to secure the right growth rates is also essential. To make up for lost time in regard to these, Wilkins points out that it may be necessary to keep the cretin for a time mildly hyperthyroid. In my clinic the experience has been the same.

The magnitude of dosage that may achieve the desired ends is somewhat as follows:

Age	*Dosage*
2- 4 months	1/10 grain per day
4- 8 "	1/5 grain per day
8-12 "	3/10 grain per day
12-24 "	2/5 to ¾ grain per day
2- 4 years	½ to 1½ grains per day
4-12 "	1 to 3 grains per day

The reports of success with treatment vary. Certainly no amount of treatment will make the cretin more intelligent than he would have been had he not been a cretin, and in the experience of several competent observers, even with seemingly good treatment, a distressing number of cretins end up with mental ages of not over ten or eleven years, although in other respects they become quite normal adults. None the less a few do better than this; and a mental age of ten or eleven with a normal body is vastly to be preferred to the state of imbecilic dwarfism that would persist if no treatment, or inadequate or unsustained treatment, were given.

When myxedema is acquired in childhood, the child having made a normal growth in all respects up to the time hypothyroidism supervened, the results of treatment are nearly as perfect as in adult myxedema. In order to make accurate predictions of what may be expected of treatment, therefore, it is necessary to distinguish sharply in diagnosis between cretinism and juvenile myxedema. This should not be difficult because the child who has acquired myxedema does not possess the dwarfism and gross habitus of the cretin, but merely the dry skin, puffi-

ness and retardation displayed by the adult with myxedema.

In conclusion I urge you to be on the look-out for all types of hypothyroidism, for it is most unfortunate to miss the diagnosis of a curable disease. In treating adults with myxedema, be watchful for untoward effects during the inauguration of therapy, and reduce the dose of thyroid if they occur. With regard to cretins, the important points are very early diagnosis, and sustained and sufficiently large dosage of thyroid throughout life.

REFERENCES

1. Castleman, B. and Hertz, S. Pituitary fibrosis and myxedema, *Arch. Path.*, 1939, *27:* 69.
2. Talbot, F. B. and Moriarty, M. E. The value of basal metabolism in the diagnosis and treatment of cretinism, *Am. J. Dis. Child.*, 1923, *25:* 183.
3. Wilkins, L. The rates of growth, osseous development and mental development in cretins as a guide to thyroid treatment, *J. Pediat.*, 1938, *12:* 429.

THE MODERN TREATMENT OF PYOGENIC OSTEOMYELITIS*

DALLAS B. PHEMISTER

Professor of Surgery, University of Chicago

WHEN a new treatment of pyogenic infection such as sulfanilamide is introduced, it is always appropriate to consider it in relation to osteomyelitis because of the high mortality, prolonged morbidity, resistance to treatment, and marked tendency to recurrence, characteristic of this disease. I have not had a great experience with sulfanilamide but I shall take advantage of the occasion to review the general field of osteomyelitis therapy which is the subject of much controversy.

The reason for the difficulties encountered in the treatment of osteomyelitis is to be found mainly in the nature of bone itself. The infection begins within a rigid tube which offers resistance to external drainage and invites spread along the medullary canal with death of bone. The presence of lime salts in the dead bone causes it to be broken down much more slowly than soft tissue and only by the direct cellular action: sequestrated parts are either extruded or have to be surgically removed. The persistence of cavities, large and small, which remain the seat of infection, leads to a state of chronic osteomyelitis and is responsible for recurrences. The infected bone cannot be completely excised, as in the case of an infected viscus, such as the appendix, because of danger of creating a defect. Another difficulty is that osteomyelitis is due to the staphylococcus in about 90 per cent of the cases and the body is particularly slow to develop an immunity against infection by that organism.

If we review the pathogenesis, the portal of entry of the organism cannot be detected in about 75 per cent of the cases, but in the other 25 per cent it is known to be a local infection usually of the skin, less often in the respiratory tract. In the other 75 per cent it is presumably a small hidden point of infection. Micro-organisms are fed into the blood stream from here, lodging in the sinusoids, or possibly in clumps as small emboli, and setting up infection in the bone. Large septic emboli rarely

* Read October 5, 1939 at The New York Academy of Medicine, in a Symposium on "The Treatment of Pyogenic Infections with Special Reference to Chemotherapy."

lodge in bone creating massive infarction and osteomyelitis. In some cases bacteria lodge in other structures as well and simultaneously give rise to sepsis. In the great majority of cases this is not so. They set up only osteomyelitis.

The evolution of the osteomyelitic focus is then an extremely variable one. In severe cases it spreads rapidly, destroys the bone extensively, and in turn may give rise to sepsis. From this group of severe cases the grade of inflammation may range all the way down to a localized osteomyelitis with slight local and general symptoms. Because of this marked variation in extent and severity, it is difficult to discuss the treatment in brief general terms and each case calls for more or less individual consideration.

Septic cases: Osteomyelitis as a part of a widespread sepsis does not call for operative treatment. It should be treated by fluid administration, by blood transfusions and, in the present opinion of the profession, by sulfanilamide or derivatives. How successful the drug will be is still uncertain but it is doubtful if cures will be effected. Long states that in staphylococcus sepsis little is to be expected from its use. If abscesses point they should be drained.

Severe cases that are primarily osteomyelitis fall into two age groups: infants and children; adults.

Osteomyelitis in infants and very young children differs considerably in etiology, pathology and clinical course from that in older individuals and its treatment is somewhat different. It is due to hemolytic streptococci in about 50 per cent of the cases. The lesion is more often localized to the end of the shaft, although multiple involvement is common. A reason for this is that the cortex is thin and permeable and the pus quickly breaks through, forming a peripheral abscess. The children are usually very sick at the onset.

Treatment should consist of fluid administration, blood transfusions, sulfanilamide and immobilization of the affected part. Operation is badly tolerated and should be postponed until abscesses form which should be opened through small incisions. There is rarely necessity for early opening of the bone for drainage of abscess even in mild cases. Dead bone is absorbed rapidly, cavities fill out and in three or four months the bone is restored to normal as shown by roentgenograms.

Severe osteomyelitis in older children and adults should be treated expectantly in its early stages by parenteral fluids, blood transfusions,

sulfanilamide and immobilization. In eighteen cases of staphylococcus osteomyelitis treated by sulfanilamide the results were doubtful. Very early operation for opening the bone before extension of the infection to the outside has occurred is usually more dangerous than helpful. Practically most cases do not offer the surgeon the opportunity of early operation because they are sent to the hospital later after abscesses have formed.

Usually pus will localize and appear external to the bone in from three to seven days. Aspiration is a helpful adjunct in detecting it. When the abscess can be located, it should be opened and drained with small single or multiple incisions and as little anesthesia and blood loss as possible. Local anesthesia may frequently be employed. However, if the patient continues very ill and external pus does not appear within a few days, do not hesitate to operate, making an opening through cortex and draining the medulla. Failure to do so may mean marked spread of the infection and necrosis of the bone, and in some cases the development of septicemia.

Milder forms of acute osteomyelitis and especially the localized abscesses in which the general symptoms are not marked call for less urgent treatment, and are usually seen by the surgeon at an even later date than the severe cases. As soon as the lesion can be definitely localized with roentgenograms or otherwise, it should be drained and the cavity effaced, as the earlier this is done, the less the likelihood of establishment of a chronic osteomyelitis.

Secondary foci of osteomyelitis are common, beginning days to years after the onset of the primary focus.

The great majority of them are localized lesions and they often develop with mild local symptoms or even silently. I have seen many instances where weeks or months elapsed before they caused local symptoms or a local swelling and where they were discovered incidentally in roentgenograms. They should be treated by the same operative procedure as is used for the primary cases.

The treatment of the subacute and chronic stages of osteomyelitis is the subject of much less dispute than is that of the acute stage. Sulfanilamide usually has no influence on the condition, although I have seen a few cases where rapid healing followed its use. By far the most important point is the performance at the earliest possible time of a thorough operation, for the removal of dead bone and the effacement of cavities,

pockets and bone sinuses. As much chronically infected bone should be removed as is compatible with preservation of continuity of the shaft. Subperiosteal resection results in interruption of continuity so often that it is rarely indicated except in the ribs, upper portion of ilium and fibula where it should be used routinely since the creation of a defect in those regions makes no difference.

The type of dressing employed afterward is of minor importance. The wound may be packed open for three to six days and afterwards dressed with surface dressings. Cast immobilization is indicated in case of large wounds. The wound may be dressed with an Orr vaseline pack and a cast applied with changes of the pack every four to six weeks. This latter method is often a very annoying and unpleasant form of treatment. I can see no fundamental virtue in it and do not use it. Cases thus treated heal as well but no better than those treated by the first method.

I have said nothing of vaccines, serums, maggots, and bacteriophage in the treatment of either acute, or chronic osteomyelitis. None of them seems to have proven sufficiently practical or to have given sufficiently satisfactory results to have won a general and lasting place in osteomyelitis therapy. Personally, I do not try to use any of them.

In closing, I realize that this discussion of the treatment of osteomyelitis has been very incomplete and I have mentioned few of the technical aspects of the problem but I have tried to select only those features which I considered most appropriate for this program.

OTITIS MEDIA AND ITS EXTENSIONS*

EDMUND PRINCE FOWLER, JR.

Assistant Clinical Professor of Otolaryngology, College of Physicians and Surgeons, Columbia University

THE title of this paper may seem strange to some. It is based on the consideration that mastoiditis, petrositis, labyrinthitis, Bezold's abscess, sinus thrombosis, and brain abscess, as well as meningitis of otic origin, are simply "extensions" of otitis media. The middle ear is the primary focus and also the most important drainage point, hence the emphasis will be on it rather than on other parts.

To understand the chemotherapy of otitis media and its extensions it is necessary to know something of the average course of the disease and something of the development and detailed anatomy of the temporal bone. As every physician knows, the latter consists of relatively flat outer parts called the squamous and mastoid portions from which projects inward a roughly three-sided structure called the petrous pyramid. This pyramid is the most important part of the temporal bone because it forms the keystone of the base of the skull and contains the middle ear and labyrinth. The labyrinth will not concern us in this paper because it is only secondarily involved in infections of the temporal bone. We are here only interested in the primary infections. As mentioned above, these spring almost invariably from the middle ear, although blood stream infections from distant foci have been described.

Simply stated, the external auditory meatus develops from the first branchial cleft, while the middle ear and Eustachian tube develop from the first branchial pouch. The lining of the middle ear cavity, therefore, is made up of mesoderm and entoderm which is continuous with mesoderm and entoderm of the nasopharynx. The ear drum is the partition between the outside and inside invagination and consists therefore, not only of the lining of the middle ear but also of the stratified squamous epithelium which develops from the ectoderm of the embryo. Now at birth, the middle-ear cavity is almost entirely filled with mesoderm, but

* Presented October 5, 1939 at The New York Academy of Medicine in the Symposium on "The Treatment of Pyogenic Infections with Special Reference to Chemotherapy."

as the individual grows this becomes thinner and thinner, so that in adults the submucosal tissues are so thin that they lie directly on the underlying bone. This single, rather flat-celled layer of epithelium and its underlying connective tissue is therefore often called "mucoperiosteum."

At birth the petrous pyramid, exclusive of the middle ear cavity, consists of bone, labyrinth, fibroblastic marrow and spaces for blood vessels. As the temporal bone grows, the fibroblastic marrow begins to be replaced by air-filled mucous membrane which pushes out in all directions, but most extensively through the antrum, into the mastoid and thence into the squamous portions of the bone.

Just how far this process will go in a given, growing child we have no means of prediction. In the opinion of the author, normal pneumatization of the temporal bone is largely a matter of the hereditary formation of the skull. Perhaps the size of the brain has something to do with it (cf. the studies of Dyke and Davidorf in cases of hemiatrophy of the brain). The generally accepted theory is that of Wittmaack who believes that reduced pneumatization is due to early infection of the mucous membrane which prevents normal invagination of the air-filled middle-ear sac. Others present different theories. Actually, we do not know any more about why some mastoids are large and highly pneumatized than we do about why some feet are big and flat while others are small and arched. There are undoubtedly many factors, some normal, some pathologic, which contribute to the final result. However, it makes a great difference whether the temporal bone is highly pneumatized or not. The great surface presented by many air cells lined with mucous membrane can excrete entirely too much fluid, if inflamed, to evacuate through the Eustachian tube or through a perforation in the drum membrane. Extension of the inflammation and pain due to the pressure are the result. Furthermore, if the temporal bone is extensively pneumatized, there is more chance for infection to become shut off at a distant point where drainage through the middle ear is impossible. It is these cases which often come to mastoid surgery or to surgery deeper in the temporal bone.

It must be remembered, to understand the foregoing discussion, that the middle ear is actually not a small cavity with specific dimensions as is intimated in most text books. Actually, it is almost impossible to measure the capacity of the middle ear because air cells in and around it

Fig. 1—Vertical section through four temporal bones at the depth of the round and oval windows showing the variation in the size of the middle ear cavity and the communication of the middle ear cavity with surrounding air cells.

vary so tremendously from case to case (Fig. 1). When the middle ear becomes infected, these air cells also become infected so that it is impossible to have otitis media without some mastoiditis, and if the petrosa is pneumatized, impossible to have otitis media without some petrositis. The air cells allow the infectious processes to involve at once a large part of the temporal bone. Their partitions are thin and are normally poorly vascularized, and worse than this, their connections are usually relatively small. It is really a wonder that infections of the mastoid so often get well without surgery. Furthermore, the air cells, especially in children, abut directly on bone marrow, and in certain types of infection, this becomes involved in the disease. It has not yet been ascertained

Fig. 2—Photomicrograph showing mild, low-grade inflammation in the niche of the oval window.

whether it is the increased vascularization and local leukocytosis of inflammation which permits the body to take care of such poorly drained areas, or whether it is a stifling of the growth of the invading organism by the production of anaerobic conditions. Conceivably all of these factors and perhaps more are responsible.

Mode of Infection in Otitis Media

The complicated series of cavities in the temporal bone can become infected in a number of ways. In infants, the most usual way is for the nasal secretions to run into the Eustachian tubes as the child lies on his back during an upper respiratory infection. Very small children cannot blow their noses or hawk mucus from their nasopharynxes, and since their Eustachian tubes are relatively short and straight, infection easily

Fig. 3—More advanced stage of inflammation in the niche of the oval window. Note increased vascularization and thickness of the mucous membrane about the anterior crus of the stapes.

enters their middle ears. If they are turned on their bellies, however, it may easily drain out again. There is much less suppurative otitis media in the infant wards where babies are turned over regularly. With older children and with adults, the commonest method of infecting the middle ear seems to be from blowing the nose too violently. Marked sudden changes in pressure, such as those produced by deep diving may also suck infected material from the nasopharynx into the middle ear. Occasionally an ear drum becomes perforated or ruptured, permitting infection from the external canal to enter the middle ear, but even in these cases the usual cause of the infection is the nasopharynx. The perforation in the drum makes it very much easier to blow infected material

into the ear because there is no longer a closed cavity. How much infection of the middle ear takes place through the submucosa of the Eustachian tube due to its contiguity with the nasopharyngeal lining is still a matter of conjecture.

Pathology of Otitis Media

Regardless of how an infection enters the middle ear, the pathology is at first the same. There is edema of the mucous membrane, which swells five to ten times the normal thickness, then a serous effusion into the cavity. Following this there is a leukocytic infiltration of the submucosa beginning perivascularly and then extending to involve the entire mucoperiosteum. As time goes on, the effusion into the cavity tends to become purulent. At first, polymorphonuclears are quite prominent, but soon very few can be found among the monocytes. As fluid and sometimes gas collects in the cavity, the drum bulges outward and more and more of the surrounding cells become involved. The more virulent the infection in the submucosa, the more quickly the effusions become purulent, and the more reaction produced not only in the middle ear but also in the surrounding air spaces. If the infection is fulminating, the drum either ruptures spontaneously or has to be opened by a surgeon. Drainage is effected, and as a rule there is subsidence of the process in four to thirty days. Very mild processes, however, have been known to subside in twenty-four hours, but occasionally there is a smoldering infection which does not subside for several months. If the infection in the main cavity persists more than a few days, it almost invariably becomes more purulent, spreads and pockets in several places producing a thrombophlebitis of small veins in the mastoid and petrosa and thereby brings about necrosis of the air cell system. Excessive fluids secreted by the mucous membrane may also produce destruction of the bone by direct pressure. Microscopic sections show the mucoperiosteum of both middle ear and mastoid cells to be densely packed with leukocytes and fibroblasts. There is also destruction of the epithelium at various points and consequent invasion of the cavities with granulation tissue. With the breaking down of bone there is always some regrowth of osteoid, but in progressing empyema the regrowth of bone lags behind the breaking down. The cortex of the temporal bone may erode at any point, producing an abscess behind the auricle, over the lateral

Fig. 4—Still more advanced inflammation in the region of the round window and beginning polypoid degeneration

sinus, in one of the cranial fossae, or even in the neck, cheek, or nasopharynx. The more extensive the air spaces, the more chance of infected material becoming caught in some out of the way pocket and so producing a focus which will seek drainage by breaking through the cortex in this way. No matter how extensive the pneumatization, however, there is always some marrow in the temporal bone which is contiguous with the most peripheral air spaces. With infection of the air spaces there is always some reaction in this marrow, and occasionally, especially in young bones, the infection actually invades the marrow spaces, producing an osteomyelitis.

For purposes of simplification, then, the pathology of otitis media and its extensions can be divided into four distinct steps: first, edema of the mucoperiosteum and serous exudation; second, increased vascu-

larization of the submucosa, infiltration with leukocytes, proliferation of fibroblasts and increased purulency in the exudation; third, after two or three weeks, necrosis of the soft tissues as well as the bony walls of the cavity (this can now be seen in roentgenograms); fourth, especially if the process is less fulminating, there may develop polypoid degeneration of the mucoperiosteum and a prolonged, low-grade osteitis and osteomyelitis.

Any one of these four processes may stop, regress, and heal, leaving a more fibrotic mucous membrane and organized bands of scar tissue attached to the ossicles. Usually there is some reduction in size of the air cavities which already exist, and in young children infections may inhibit further pneumatization of the mastoid.

With repeated infections the processes are very similar in each instance except that inflammation in previously formed scar tissue produces much less vascularization than in normal tissue. The scar tissue may toughen the drum so that it does not break. Pressure then builds up in the middle ear and spreads the infection more deeply. Furthermore, with the regrowth of bone in the previous infections the connection between the mastoid cells as well as the antrum is likely to be narrowed. This increases the possibility of infection becoming trapped deep within the bone, and explains why complications most often occur in cases with a history of previous otitis media.

Therapy of Otitis Media

The treatment of otitis media for the last several decades has been directed towards the provision of adequate drainage for the middle ear and its surrounding air cells. If the infection was mild (so-called "acute-catarrhal" otitis media) drainage was usually obtained by reduction of infected material in the nose and by shrinkage of the Eustachian tube orifice. If the infection was more acute or more purulent, incision of the drum was resorted to. After myringotomy or spontaneous puncture the canal was simply kept clean to promote drainage either with dry wipes or irrigations of various kinds. If these did not suffice and the mastoid was seen to be breaking down in the roentgenogram, a mastoidectomy was performed, usually in the third or the fourth week of the infection.

Since 1936 the use of sulfanilamide and related drugs has been added to our resources. A great many cases show subsidence of symp-

TABLE I

FACTORS IN OTITIS MEDIA

1. Age: Infants and old people apparently more susceptible.
2. Sex: No essential difference.
3. Place: Flora and fauna vary in different vicinities.
4. Environment
5. Station in Life: Clinic patients seem to have more trouble than private patients.
6. Habits: Blowing of nose, swimming, etc.
7. Diet: Vitamins, etc.
8. Previous Infection and Immunity to Infection.
9. Mode of Infection
10. Time: Yearly cycles of incidence, March and April peak, etc.
11. General Physical Condition: Debilitating disease.
    Allergy.
12. Heredity: Race.
    Susceptibility to infection.
    Anatomy:
        Pneumatization of the temporal bone.
        Type of Eustachian tube.
        Lymphoid diathesis.
13. Skill of Physician and of Nursing.
14. Reaction to Surgery.
15. Reaction to Medication: Sensitivity.
    Tolerance:
        Vomiting.
        Excretion, etc.
    Individual Response.
16. Type of Infection.
17. *Chance.*

toms after chemotherapy so that many physicians have come to believe that it is the only treatment for otitis media, and are beginning to use it in every case. Even the lay public often asks that it be prescribed.

The bad results from improperly conducted chemotherapy often reach the hands of the otologist, so that he tends towards the opinion that drugs are of questionable value. Certainly the present ones mask symptomatology, sometimes cause unpleasant reactions, and make the problems of management harder for him. We have, then, on one side the general doctor and the pediatrician who tend to treat all types of otitis media (often even the non-suppurative types) with chemotherapy, and on the other the otologist who uses it only in desperate cases such as meningitis. Which is correct? Is there a middle ground? Is there some

rule which has scientific rationale, and which will work in the majority of cases? I believe that the rule can be built out of a study of the normal course of the disease, the pathology outlined above, and the results obtained in various types of cases by various methods of administration.

As already intimated, there are a great many factors which may influence the course of otitis media. These are summarized in Table I. Many have never been thoroughly studied, but a little thought about each one will tend to give it proper significance.

A word is perhaps necessary for certain items: under Heredity we have listed Anatomy, which is divided into pneumatization (already discussed) and Eustachian tubes, diameter, and curvature. Very little is known on this last subject except that certain people seem to have much more trouble with their tubes than others. It is also known that excessive lymphoid tissue about the tube seems to be an hereditary trait, and that this tissue tends to stop up the tubes and predispose to otitis media unless proper measures such as adenoidectomy or radiotherapy are used to combat it. Certainly the use of chemotherapy has not yet precluded the necessity for adenoidectomy in cases of recurrent otitis media.

It may surprise some to see a heading *Susceptibility to Infection* under Heredity. The work of Webster at the Rockefeller Institute, however, has definitely established this for mouse typhoid and mouse encephalitis, and the author has found hereditary susceptibility for otitis media in rats which could be bred out of a colony. There is no doubt that otitis media seems to run through certain human families.

Types of Infection

Table II shows that we have a specific chemotherapy for less than half of the total number of cases of otitis media. For over 35 per cent of the cases are due to the staphylococcus and more than 15 per cent are due to other organisms for which no specific chemotherapy has as yet been developed. However, about 30 per cent are due to the hemolytic streptococcus for which we have sulfanilamide, and 12 to 16 per cent are due to pneumococci for which we now have sulfapyridine. Study of Table III will show that three-quarters of the pneumococcus and streptococcus cases get well within three weeks without chemotherapy. These two tables indicate clearly that the group that needs to be treated with chemotherapy is definitely a small one.

TABLE II

PERCENTAGE OF VARIOUS ORGANISMS FOUND IN PURE CULTURE AT THE COLUMBIA PRESBYTERIAN MEDICAL CENTER IN THE YEARS 1933 TO 1939

Year	*Strep Hemo*	*Strep Other*	*Pneumo I*	*Pneumo III*	*Pneumo Other*	*Staph All Types*	*Others*
1933 273 cases	31.13	4.39	2.56	6.22	4.02	41.75	9.89
1934 334 cases	35.2	3.3	3.0	5.7	3.6	41.8	7.8
1935 333 cases	34.6	1.8	4.2	8.1	9.0	32.7	9.6
1936 336 cases	33.1	2.6	8.0	11.9	10.4	27.4	6.6
1937 517 cases	38.7	2.5	3.7	5.0	9.3	33.5	7.3
1938 524 cases	26.44	3.66	5.2	4.63	5.5	41.50	14.9
1939 438 cases	36.78	.91	4.1	5.51	6.4	36.78	10.11
Total 2,755 cases	33.6	2.7	4.45	6.4	7.04	36.7	9.5

TABLE III

DURATION OF DISCHARGE AND NUMBER OF PATIENTS THAT CAME TO MASTOIDECTOMY OUT OF 455 CASES DIAGNOSED AS OTITIS MEDIA, ACUTE SUPPURATIVE, IN THE COLUMBIA PRESBYTERIAN MEDICAL CENTER FROM MAY 1936 TO MAY 1937

	1-6 days	*7-14 days*	*15-21 days*	*3-4 weeks*	*More than 4 weeks*	*Mastoid-ectomy*
Staph 173 cases	26	62	18	27	33	7
Hemo Strep 163 cases	22	42	21	22	26	30
Pneumo 101 cases	16	28	20	12	12	13
Other Organisms 20 cases	4	9	1	4	0	2

In all fairness it must be pointed out, however, that there is a flaw in the above argument. It assumes that the culture reports are accurate. As a matter of fact, the figures are undoubtedly not exact, for unfortunately many of the cultures were taken using a swab without sterilization of the external auditory meatus. (Incidentally it has been shown by Page that throat cultures are often apt to pick up the offending

pathogen more accurately than a careless swabbing in the external canal.) However, the cultures described above were all made in suppurative cases, and if one adds to these the non-cultured cases, especially the non-suppurative cases, it is still fair to say that in the present state of our knowledge chemotherapy is indicated for only a small percentage of all the cases of otitis media.

How shall the surgeon discover this small percentage? Can it be determined with our present meager knowledge of the action of the drug and our knowledge of the pathology of otitis media? Lockwood and others have definitely shown that sulfanilamide is less efficient in necrotic lesions, and that the more the necrosis, the less the likelihood that the drug will be sufficiently bacteriostatic to permit the body to annihilate it. As has been pointed out above, very little necrosis—as a rule—occurs in otitis media and mastoiditis, until the second week of the disease. It would seem, therefore, that in simple otitis media one can wait a week or ten days after the onset using the old, simple, mechanical methods of treatment. Then if there is no improvement and the case looks as if it might go on to surgical mastoiditis or a long siege of drainage, the administration of drugs may be begun with every expectation that they will stop the process if given in sufficient dosage. At the end of a week adequate bacteriological and blood studies should be available so that the correct drug can be selected. Analysis of cases treated with sulfanilamide (Table IV) shows that a large percentage of cases treated with adequate dosage, especially those in hospital, get well while those treated with small or short dosage in the clinic show no more tendency

TABLE IV

APPARENT EFFECT OF SULFANILAMIDE IN OTITIS MEDIA IN 100 UNSELECTED CASES

100 CASES	
Postoperative, questionable effect	6
Reaction	6
Recurrent	11

	Inadequate dosage	*Adequate dosage*
No effect	31	11
Questionable effect	18	3
Good effect	18	25

All but four of the cases on adequate dosage were in the hospital. "Questionable effect" represents cessation in less than two weeks. "Good effect" represents cessation of discharge in less than a week.

to recover than an untreated series (cf. Tables III and IV). The cases in which the drug has no effect are usually cases of inadequate dosage. Often there is recurrence if adequate dosage is not prolonged well after temperature is normal and drainage has stopped. If the drug is started late in the disease it may have no appreciable effect. Apparently the drug has less effect in cases where there has been a previous infection.

We have much divergence of opinion as to the dangers of chemotherapy. Many say that there is virtually no danger, especially in children, and that all drug-sensitive individuals show up on small dosage so that they can be spotted before any serious harm has been done. Others emphasize the danger of damage to the kidneys and liver; cite the patients who have died with anemia and leukocytopenia, or speculate on the effect of the drug on the reticulo-endothelial system in the years to come.

The physician must decide at the end of a week or ten days whether his case is going on to a surgical mastoiditis or is going to prolong itself enough so that the patient is in danger of acquiring a residual deafness. If he is fairly certain of one of these things, the dangers outlined above need hardly be considered. Chemotherapy should be instituted as a major procedure, comparable in every way to surgical interference. If possible, the patient should be hospitalized, and if not, careful blood and urine studies should be done every two days at home. The dosage should be fairly large (Long and Bliss suggest at least 2 mg. per kilo of body weight) and kept up for several days after the temperature has come to normal and the discharge behind the drum has ceased. If this is not done there will be almost certainly a recurrence of the disease, especially when the original organism is a virulent one.

Analysis of successful sulfanilamide-treated cases shows a dramatic subsidence of symptoms within three or four days. Most of them have no pain or fever after two days. This suggests that if there is no effect within three or four days the drug is not the answer, and that drainage will have to be instituted by one of the well-known surgical methods. In advanced or neglected cases surgery is usually essential, but of course may be supplemented by chemotherapy. After all, it is impossible to drain every nook and cranny in the temporal bone, and the chemotherapy will produce bacteriostasis in these unreachable regions. The combined use of surgery and chemotherapy is especially important in the complications of otitis media such as meningitis, brain abscess, and

inflammation of the walls of the venous channels draining the temporal bone.

To recapitulate, given a case of otitis media, chemotherapy should be instigated a week or ten days after the onset of the disease, if the patient does not seem to be getting well without it and a specific drug is available to combat the bacteria of the infection. The chemotherapy must be given in adequate dosage for a considerable period after symptoms begin to disappear and under careful surveillance of reactions and with surgical adjuncts to the therapy in mind. In no case should it be given casually, without cultures and without a knowledge that most otitis media is self-limiting. It must be remembered that the use of bacteriostatic drugs makes the management of the cases harder because the symptomatology of the disease processes is masked.

Some day it is hoped that we will have new drugs for all types of infection, and drugs which can be given without untoward outside effects—then of course, the above working rule for our present drugs will have to be modified.

OBSTETRICS AT THE NEW YORK ALMSHOUSE AND AT BELLEVUE HOSPITAL*

CLAUDE EDWIN HEATON

Assistant Visiting Gynecologist and Obstetrician, Bellevue Hospital

IN colonial times the care of mother and child was entirely in the hands of midwives. The midwives of New Amsterdam were no better and no worse than their professional sisters in Holland who aroused the ire of Hendrick Van Deventer. The father of modern midwifery wrote: "they do not understand their business;" and again he lamented "I cannot sufficiently wonder at the gross ignorance of most midwives." He urged that examination of the bodies of women dying in childbirth be made a matter of law, to find out whether the mother and fetus died naturally or "sadly perished by the carelessness and cruel hand of the midwife."

The midwives of New Amsterdam have been classed by some writers among the Zeikenstroosters or comforters of the sick. The Zeikenstroosters, however, were men and their function was purely spiritual although they occasionally looked after the sick in defiance of an ecclesiastical ruling prohibiting them from practicing medicine.

Improvement in American obstetrics did not take place until just prior to the Revolution when young colonial physicians began to go abroad for study. The eighteenth century was a period of remarkable growth in the specialty. Knowledge of the obstetrical forceps enabled physicians to displace the Sairey Gamps who had reigned so long in the lying-in chamber. The most potent factor in the manifold advances of the period was the rise of the new humanitarian spirit. As part of this the infant welfare movement emerged. "In the nurture and management of infants as well as in the treatment of lying-in women," wrote Lettsom in his *Medical Memoirs* in 1774, "the reformation hath equalled that in the smallpox; by these two circumstances alone incredible numbers have been rescued from the grave."

* Read January 11, 1939 at The New York Academy of Medicine before the Section on Historical and Cultural Medicine.

Among those studying abroad were William Shippen, Jr., of Philadelphia, James Lloyd of Boston and Samuel Bard of New York. They returned from Edinburgh and London filled with inspiration by their contact with great clinical obstetricians like William Smellie and William Hunter. Each one became the pioneer teacher of obstetrics in his community. Dr. Samuel Bard emulating Dr. John Morgan of Philadelphia, organized the medical school at Kings College (later Columbia) in 1769. At the first Commencement he urged in a notable discourse the usefulness and necessity of a public hospital. This address led to the founding of the New York Hospital, which was chartered in 1771 but did not open for the reception of patients until January 3rd, 1791. Delay during the reconstruction period in the re-establishment of the Medical School and the opening of the hospital was undoubtedly due to divided loyalties engendered in the medical profession by the struggle for Independence.

In 1736, a new Almshouse was built on the Commons where the City Hall now stands. Here according to Dr. Robert Carlisle was the primitive trace of Bellevue Hospital. Following the war the Almshouse was utilized for the first clinical teaching in New York. Both Valentine Seaman and David Hosack studied at the city Almshouse which according to Dr. J. W. Francis was "at that time the only institution in New York in which medical instruction was imparted." Dr. Nicholas Romayne, Dr. Benjamin Kissam and Dr. William Moore were visiting physicians and Dr. Wright Post, the visiting surgeon.

We read that Dr. William Moore's attention "was always more specially directed to the practice of Midwifery, in which he acquired a very extensive experience and practiced with great success, keeping a record of all cases which he attended for the year 1781 to 1823, which amounted to nearly 3,000 cases."

A new Almshouse was built on Chambers Street in 1796. Here the first lying-in hospital in New York City was established in 1799. The previous year a severe epidemic of yellow fever had swept the city. Many expectant mothers lost their husbands. Their pitiful condition aroused the sympathy of Dr. David Hosack. Through his efforts the New York Lying-In Hospital was incorporated in February, 1799. A place was secured at No. 2 Cedar Street and an appeal for subscriptions was made in the Commercial Advertiser for July 23, 1799. In the Medical Repository for 1800, under "New York Lying-In" is the note:

"We are informed that this Hospital will be ready for the reception of patients on the first of August."

Prior to the opening of the institution on Cedar Street a lying-in ward was opened in the Almshouse Hospital on Chambers Street. The Medical Repository for May, 1799 states that:

"A lying-in ward has been established in the Almshouse of the city of New York. The cases which occur there are numerous enough to answer the purpose of public instruction. Accordingly, there is delivered a course of lectures on the obstetric art, including the anatomical, physiological, and practical parts, by Valentine Seaman, M.D. As this establishment is particularly and exclusively devoted to the education of *females*, it will be easy for *women* who practice, or intend to practice midwifery, to avail themselves of the excellent opportunities which are hereby held out to them."

The following year Valentine Seaman published the first book to appear on the subject of midwifery by an American author. On the title page he calls himself Physician Extraordinary to the Lying-In Ward in the Almshouse. The little volume bears the quaint title, *The Midwives Monitor and Mothers Mirror*, and the contents are based upon the course of instruction given the previous winter in the lying-in wards of the Almshouse. Thus to the forerunner of Bellevue Hospital belongs the honor of establishing the first wards in New York for expectant mothers and of giving the first hospital instructions to women in the art of midwifery.

The statement has been repeatedly made that Dr. Valentine Seaman gave a course for trained nurses at the New York Hospital in 1800. The sole authority for this is a letter beneath his portrait in which a member of the family wrote that he gave a course of lectures to the nurses of the New York Hospital. The lectures referred to were obviously those given during the previous winter in the Almshouse as he himself states in his book.

The first outdoor obstetrical service in New York was established by the New York County Medical Society in 1823. On June 2 a committee was appointed by the Society, "to inquire into the cause of the great number of stillbirths in this city." The Chairman of the Committee was Dr. Charles Drake, one of the visiting physicians to Bellevue Hospital. The Committee was of the opinion that among the reasons for the large number of stillbirths was the abuse of ergot and the fact

"that the practice of midwifery was still too much confined to ignorant and inexperienced attendants." The Committee recommended "the institution of a lying-in charity for the exclusive purpose of attending parturient females at their own homes." In the minutes of the New York County Society are the regulations drawn up for the Out-door Lying-In Charity. A group of consulting and attending accoucheurs were appointed for the various districts in the city to attend the poor in their own homes.

In order that the new project should be "more effectively guarded against producing injury to any part of the profession who now receive a compensation however small from attendance upon the lower classes of the community," it was decided "that it shall be the duty of the attending accoucheurs to lodge with the Commissioners of the Almshouse a notice of their respective residences, to attend during childbirth, free of all charge, such females of their respective districts as shall produce a certificate from a Commissioner of the Almshouse of their being proper objects of charity, and to report at the ensuing anniversary meeting of the Society the number of cases they have attended, the character of each labor, together with such other circumstances as they shall deem worthy of being communicated."

The out-door obstetrical service functioned for only a short time. The New York Lying-In Hospital which had closed in 1822 again opened a ward in the New York Hospital sharing its facilities with the New York Asylum for Lying-In Women established in 1822. The latter institution moved to a house on Marion Street in 1830 and in addition to an indoor service established a large outdoor service. It was known as the old Marion Street Maternity Hospital and eventually combined in 1899 with the New York Infant Asylum (incorporated in 1865). The New York Infant Asylum combined with the Nursery and Child's Hospital (incorporated in 1854) to form in 1910 the New York Nursery and Child's Hospital.

One of the early New York obstetricians whose name is closely associated with Bellevue Hospital was Dr. John Wakefield Francis. He was born the year of Washington's inauguration and died the year the Civil War started. For years he was *the* doctor of New York City and his big bushy head was as familiar as the City Hall. While still a student of Dr. David Hosack whose partner he later became, Francis helped establish the *American Medical and Philosophical Register*. The delight-

ful tone of this early magazine was due in a large measure to the literary ability of Francis. His scientific attainments were perhaps few but he was a popular teacher and to his associates in the profession he was "our beloved Francis," a man who was, according to Jacobi, keen eyed, warm hearted, plain spoken and generous minded.

Dr. Francis' house, No. 1 Bond Street at the corner of Broadway was the rendezvous for all the leading lights of the city. His book of reminiscences, *Old New York*, is a storehouse of information about the last days of Knickerbocker New York. There are many amusing stories about Dr. Francis. He continued to bleed his patients long after most of his confrères had given up the practice. Once during a dinner party at his house he suddenly left the table and called his wife to an adjoining room where he proceeded to bleed her. In answer to her protests he said that he perceived that she was about to suffer a stroke of apoplexy and deemed it best to avert it!

Dr. Emmet tells an interesting story about Dr. Francis. One of his best patients had been delivered of a baby when he had not even suspected pregnancy. He had been sent for at the time of the event but being away from home, someone in the neighborhood had attended the case. "Damn these hoopskirts," Dr. Francis exclaimed, "there was a time when I went to church that I could look around me and form some idea of what my income might be during the year. But now, since the invention of these damn hoopskirts, I can no longer judge of the condition of the women. I am away from home when wanted, and some young whipper-snapper is called in and gets the case."

Dr. Jacobi tells how, when he first started practice, Dr. Francis stopped him on the street one day. "They speak well of you," he said, "and you will get on; only people want sometimes some outward show. Now I am an old man, and you will not mind it when I say you ought to have another tailor." Jacobi replied, "you see, Dr. Francis, you are an old doctor, and famous, and you can afford to wear the old-fashioned clothing of the eighteenth of Brumaire and of the century of William Penn, but I cannot afford yet a better tailor."

Dr. Francis was one of the editors of the *New York Medical and Physical Journal* which was established in 1822. In the first number, one finds several contributions on obstetrics by Bellevue doctors. Francis himself contributed an article on *Phlegmasia Dolens*. Dr. Jacob Dyckman, one of the visiting surgeons to the Almshouse, wrote on a *A Case*

of Tumour within the Pelvis Preventing Parturition. Dr. William Moore reported *A case of uterine hydatids.* The following year Francis published a letter from John D. Hunter who while a captive among the Indians west of the Mississippi made some interesting observations on female diseases occurring among the squaws. There is also an interesting report by Drs. Francis and Beck of the first cesarean performed in the state of New York, the patient operating upon herself and recovering.

In 1825, Dr. Charles Drake, physician to the Bellevue Establishment reported *A Case of Exostosis of the Os Ischium Impeding Delivery.* The patient died of ruptured uterus.

An interesting article appeared in 1840 entitled, *A Report of Cases of Puerperal Fever Occurring at the New York Almshouse,* by Alexander F. Vache, M.D., the resident physician. The disease appeared on January 12. Of eighteen women confined in the Almshouse nine had fever and seven died. The next six women were placed in the Nursery. Of these five had fever and five died. Patients were then confined in the building devoted to negroes; out of twelve deliveries, four had fever and four died. The obstetrical service was now moved to apartments in the "middle house" of the "lunatic asylum" on Blackwell's Island. Here there were twenty-three deliveries with six cases of fever and three deaths. The total death rate during this epidemic was 31 per cent. The treatment was cupping and leeches. Among the assistants at Bellevue was Dr. Thomas F. Cock who wrote a little *Manual of Obstetrics* and became the first president of the New York Obstetrical Society.

Dr. D. Meredith Reese made a very full annual report of the Bellevue Hospital for 1848. He states that from 1845 to 1848 inclusive there were 678 births in the hospital with seventy-nine stillbirths, a rate of over 10 per cent. During the year 1848 there were 208 births with twenty-four maternal deaths of which nineteen were from puerperal fever. There were five forceps cases and six cases of embryotomy. Note that there were more destructive operations than forceps cases. Obviously a low operative incidence resulted in the loss of many babies. Fear of infection apparently deterred the doctors from interference and for the same reason cesarean section was not considered. Rupture of the uterus followed by death of the mother occurred not infrequently. From the meager records available for the twelve years from 1848 to 1859 inclusive it is apparent that the maternal and fetal death rate was

extremely high. The maternal death rate averaged ten times greater than the present rate for the city of New York and in some years it was actually twenty or thirty times greater. Puerperal infection was the chief cause of death but death from eclampsia was also common. The mortality at Bellevue was not greater than in similar institutions; there was a frightful mortality in home deliveries not only in the city but in the rural districts.

In the second half of the nineteenth century a notable group of obstetricians was associated with Bellevue Hospital. Among these were Fordyce Barker and George Elliot. They introduced the use of the hypodermic syringe in America in 1856 and 1858. They deserve our remembrance also for their defence of the use of anesthesia in obstetrics at a time when it was greatly opposed. Elliot wrote, "I would not practice medicine another day if I did not possess the power of relieving pain."

In 1876, Fordyce Barker became the first president of the American Gynecological Society. His book, *The Puerperal Diseases,* which appeared in 1874 had a deserved popularity. Barker with his immense clinical knowledge held peculiar views on the cause of puerperal infection. At the famous New York Academy of Medicine meeting in 1857 he maintained the view that it was an essential fever. Twenty years later while agreeing that it was contagious and praising the work of Oliver Wendell Holmes, he still held that the symptoms of puerperal infection were essential and not the consequence of any local lesions.

T. Gaillard Thomas was connected with Bellevue Hospital for many years. Next to J. S. Parry he did more than anyone else in this country to clarify the problem of ectopic pregnancy. He was the first in the United States to complete an extraperitoneal cesarean section. Isaac E. Taylor was a great clinical teacher and founded the Bellevue Hospital Medical College. Along with Elliot he was noted for his skill with the forceps.

With the rise of scientific medicine after 1850 the history of Bellevue Hospital becomes a part of the main current of medical history. It is probably fair to state that the influential leaders in the movement spreading from France and Germany to America were Bellevue men. The closing decades of the nineteenth century might indeed be characterized as the golden age of Bellevue for on the staff of the hospital and teaching in the medical college were the open-minded Austin Flint, Theodore

Janeway and Francis Delafield, the fathers of pathological anatomy in America; Stephen Smith and Hermann Biggs, pioneers of public health; and William Welch who was eagerly teaching the new germ theory of disease. On the surgical staff along with Smith were William Stewart Halsted, Frederick S. Dennis and Lewis Atterbury Stimson.

The big problem facing the hospital at this time was the control of infection both in surgery and obstetrics. There now appeared upon the scene a man who perhaps did as much as any other single person to make obstetrics a scientific procedure in America. William Thompson Lusk studied at Heidelberg and Berlin two years previous to 1861. At the beginning of the Civil War he returned to America and entered the Union Army. Out of his Civil War experience came his *War Letters* which were privately printed in 1911. After the war he studied at the Bellevue Medical College and then pursued further work at Edinburgh, Paris, Vienna and Prague. After a period of teaching physiology at Long Island Medical College and at Harvard he was appointed in 1871 professor of obstetrics and diseases of women and children at Bellevue Hospital Medical College, a position he held until his death.

In 1872, puerperal infection destroyed twenty-eight women of 156 who were confined in Bellevue Hospital and in 1874 from January 1 to June 11, out of 166 patients thirty-one died of infection. Lusk at this time published a clinical report on the lying-in service in which he urged the building of a separate hospital for the reception of lying-in patients. His advice was not followed but instead in 1875 the lying-in department was transferred to Blackwell's Island where two wooden pavilions were erected and placed in charge of the Charity Hospital staff. Arrangements were made by the city for several private hospitals to receive patients who came to Bellevue after labor had begun. Soon, however, these institutions refused to admit such patients. Thereupon these unfortunate women were delivered on board the transfer boat while awaiting transportation to the Island. They were attended by one of the house staff and one of the nurses from the new training school but no other provision was made for them.

At the International Medical Congress held in Philadelphia in September, 1876, Lusk read a paper entitled: *On the Nature, Origin and Prevention of Puerperal Fever.* He stated, "that the capacity of self-multiplication which septic fluids possess has been found to be coincident with the presence of certain organic bodies termed variously micrococci,

microspores, or sometimes less specifically bacteria." This statement elicited a great deal of hostility. Most teachers still believed in spontaneous generation and gave themselves scant concern about the views on puerperal infection advanced by Holmes and by Semmelweis. Lusk a few years before had heard Seyfert speak scoffingly of the misfortunes which had clouded Semmelweis' later years, asserting that his doctrines had long before been proof sufficient of his insanity.

Present as a guest at the International Congress was Lister himself who according to Lusk was listened to by a curious but unsympathetic audience. Lister visited Bellevue Hospital and complimented young Dr. Stephen Smith on his success with the antiseptic method.

Lusk himself at this period believed that there was a non-infectious form of puerperal fever due among other things to moral causes. His conclusion in regard to the infectious form, however, was that "prevention is best accomplished in hospitals by the adoption of Lister's principles," and that "the question of personal responsibility cannot be too strongly impressed upon the medical profession."

In 1877, the attention of the Grand Jury was called to the lack of facilities for obstetrical cases at Bellevue Hospital. As a result the Emergency Hospital was established at 26th Street, between Second and Third Avenues in a building which had been used as an engine house by the Fire Department. In this makeshift hospital Dr. William T. Lusk and Dr. William M. Polk began the fight to conquer puerperal infection.

Credit is due to Dr. Henry J. Garrigues for demonstrating for the first time in America in the wards of the Charity Hospital on Blackwell's Island what could be accomplished by rigid aseptic and antiseptic technique. Immediately after his first publication in 1883 Lusk introduced his methods at the Emergency Hospital and subsequently reported that there had been the greatest possible change in his service. From October, 1883 to August, 1884 there were no deaths from puerperal infection in 168 cases. Dr. W. L. Richardson at about the same time introduced the new technique at the Boston Lying-In Hospital with startling success.

In 1881, Lusk's great book on *The Science and Art of Midwifery* appeared and was translated into the French, Italian, Spanish and Arabic.

Lusk did the first successful hospital cesarean section in the United States. Harris wrote: "looking into the past records of New York City

and of the United States at large, of ten hospital cesareans in our country, Dr. Lusk's case is the first to recover up to 1887, he is the first to save both mother and child in all the history of New York, the only one of seven operators to meet with success using the Sanger Method in the United States."

Lusk died in 1897. The Emergency Hospital continued in operation until November, 1908 when Pavilions A and B of the new hospital were opened with provision for two obstetrical wards.

SOURCES

The material for this paper has been obtained in part from the following sources:

Ecclesiastical Records of the State of New York. Albany, 1901.

Emmet, Thomas Addis. Reminiscences of the Founders of the Women's Hospital Association, *New York Journal of Gynecology and Obstetrics,* May, 1893.

Garrigues, Henry Jacques. *Practical Guide in Antiseptic Midwifery in Hospitals and Private Practice.* Detroit. S. S. Davis. 1886.

Hardie, James. *The Description of the City of New York.* New York, 1827.

Harris, Robert P. Cattle-Horn Lacerations of the Abdomen and Uterus in Pregnant Women. *American Journal of Obstetrics,* Vol. 20, July, 1887.

Jacobi, Abraham. Reminiscences of Medical Practitioners in New York During the Period of the Early History of the Academy of Medicine. *Medical Record,* January 26, 1907.

New York County Society Minutes, 1806-78. Published by the Society, 1879.

LIBRARY NOTES

RECENT ACCESSIONS

"Possession does not imply approval"

Aldrich, C. A. & Aldrich, (Mrs.) M. (McCague). *Babies are human beings.*
N. Y., Macmillan, 1939, 128 p.

Alsted, G. *Studies on the changing incidence of peptic ulcer.*
Copenhagen, Munksgaard, 1939, 148 p.

Aschner, B. *Der Arzt als Schicksal!*
Zürich, Müller, [1939], 235 p.

Association for Research in Nervous and Mental Disease. *The interrelationship of mind and body.*
Balt., Williams, 1939, 381 p.

Browne, F. J. *Antenatal and postnatal care.* 3. ed.
London, Churchill, 1939, 622 p.

Brownell, K. O. *A textbook of practical nursing.*
Phil., Saunders, 1939, 418 p.

de Busscher, G. *Maag- en duodenumziekten.*
Brugge, Beyaert, 1939, 268 p.

Chance, B. *Ophthalmology.*
N. Y., Hoeber, 1939, 240 p.

Chappell, M. N. *In the name of common sense; worry and its control.*
N. Y., Macmillan, 1939, 192 p.

Clement, F. W. *Nitrous oxide-oxygen anesthesia.*
Phil., Lea, 1939, 274 p.

Congrès (2) International de Massage et des Auxiliaires Médicaux, Brussells, 1938. *Compte-rendu. . .*
Bruxelles, Sécretariat Général, [1938], 439 p.

Devraigne, L. *L'obstétrique à travers les âges.*
Paris, Doin, 1939, 128 p.

Dubs, J. *Die Feldchirurgie im Schweizerischen Gefechts-Sanitätsdienst.*
Zürich, Morgartenverlag-Aktiengesellschaft, [1939], 332 p.

Eller, J. J. *Tumors of the skin, benign and malignant.*
Phil., Lea, 1939, 607 p.

Esser, A. A. M. *Das Antlitz der Blindheit in der Antike.*
Stuttgart, Enke, 1939, 178 p.

Fifield, L. R. *Infections of the hand.* 2. ed. by P. Clarkson.
London, Lewis, 1939, 167 p.

Fomon, S. *The surgery of injury and plastic repair.*
Balt., Williams, 1939, 1409 p.

Ford, W. W. *Bacteriology.*
N. Y., Hoeber, [1939], 207 p.

Forsyth, D. *How life began; a speculative study in modern biology.*
London, Heinemann, [1939], 106 p.

Gesell, A. L. & Thompson, H. *The psychology of early growth.*
N. Y., Macmillan, 1938, 290 p.

Goldschmidt, R. B. *Physiological genetics.*
N. Y., McGraw-Hill, 1938, 375 p.

Goldsmith, M. *The trail of opium.*
London, Hale, 1939, 286 p.

Great Britain. Inter-Departmental Committee on Abortion. *Report.*
London, H. M. Sta. Off., 1939, 168 p.

Hayden, E. P. *The rectum and colon.*
Phil., Lea, 1939, 434 p.

Hodgson, (Mrs.) V. (Hoffman). *Supervision in public health nursing.*
N. Y., Commonwealth Fund, 1939, 376 p.

Internationaler (1) Kongress für gerichtliche and soziale Medizin, Bonn, 1938. *Verhandlungsbericht.*
Bonn, Scheur, 1938, 630 p.

Internationaler (16) Physiologen-Kongress, Zurich, 1938. *Kongressbericht 1-3* [*& Teilnehmerverzeichnis*].
[Basel], Freie Vereinigung Schweiz. Physiologen, [1939?], 4 pts. in 1 v.

Jackson, C. & Jackson, C. L. *Cancer of the larynx.*
Phil., Saunders, 1939, 309 p.

von Jaschke, R. T. *Die Prophylaxe auf dem Gebiet der Geburtshilfe und Gynäkologie.*

Stuttgart, Enke, 1939, 98 p.

Jones, E. *Papers on psycho-analysis.* 4. ed.
London, Baillière, 1938, 643 p.

Kaplan, I. I. & Rubenfeld, S. *A topographic atlas for X-ray therapy.*
Chic., Year Book Publishers, [1939], 55 pl.

Kummer, A. *De primaire resectie van de doorgebroken maagduodenumzweer.*
Amsterdam, Scheltema, 1939, 54 p.

Langfeldt, G. *The schizophreniform states.*
Copenhagen, Munksgaard, 1939, 134 p.

Laubry, C.; Cottenot, P. H.; Routier, D. A. [et al.]. *Radiologie clinique du coeur et des gros vaisseaux.*
Paris, Masson, 1939, 2 v.

Lewis, G. M. & Hopper, M. E. *An introduction to medical mycology.*
Chic., Year Book Publishers, [1939], 315 p.

McGregor, A. L. *A synopsis of surgical anatomy.* 4. ed.
Bristol, Wright, 1939, 664 p.

McLellan, F. C. *The neurogenic bladder.*
Springfield, Ill., Thomas, [1939], 206 p.

Marburg, O. & Helfand, M. *Injuries of the nervous system, including poisonings.*
N. Y., Veritas Press, 1939, 213 p.

Master, A. M. *The electrocardiogram and X-ray configuration of the heart.*
Phil., Lea, 1939, 222 p.

Mellanby, (Sir) E. *Recent advances in medical science.*
Cambridge [Eng.], Univ. Press, 1939, 62 p.

Mellanby, (Sir) E. *The state and medical research.*
Edinburgh, Oliver, 1939, 52 p.

Meng, H. *Seelischer Gesundheitsschutz.*
Basel, Schwabe, [1939], 223 p.

Merck (The) index. 5. ed.
Rahway, Merck & Co., 1940 [1939], 1060 p.

Mitchell, A. G.; Upham, E. K. & Wallinger, E. M. *Pediatrics and pediatric nursing.*
Phil., Saunders, 1939, 575 p.

Muncie, W. S. *Psychobiology and psychiatry.*
St. Louis, Mosby, 1939, 739 p.

New York Heart Association. Criteria Committee. *Nomenclature and criteria for diagnosis of diseases of the heart.* 4. ed.
N. Y., N. Y. Heart Assoc., 1939, 282 p.

Olivier, E. *Médecine et santé dans le Pays de Vaud au XVIIIe siècle, 1675-1798.*
Lausanne, La Concorde, 1939, v. 1.

Park, W. H. & Williams, A. W. *Pathogenic microörganisms.* 11. ed.
Phil., Lea, 1939, 1056 p.

Peiping Union Medical College. Division of Neuropsychiatry. *Social and psychological studies in neuropsychiatry in China.*
Peking, Vetch, 1939, 377 p.

Prinz, H. & Greenbaum, S. S. *Diseases of the mouth and their treatment.* 2. ed.
Phil., Lea, 1939, 670 p.

Problèmes physiopathologiques d'actualité; conférences faites par MM. Ambard, Ancel, Aron [et al.], 3. série.
Paris, Masson, 1939, 154 p.

Schulte, G. & Kuhlmann, F. *Grundlagen der Röntgendiagnostik und Röntgentherapie.*
Leipzig, Thieme, 1939, 140 p.

Schwartz, L. & Tulipan, L. *A text-book of occupational diseases of the skin.*
Phil., Lea, 1939, 799 p.

Scott, H. H. *A history of tropical medicine.*
London, Arnold, [1939], 2 v.

Smith, S. C. *Heart patients; their study and care.*
Phil., Lea, 1939, 166 p.

Stekel, W. *Technique of analytical psychotherapy.*
London, Lane, [1939], 408 p.

Surgery of the ear; S. J. Kopetzky, editor.
N. Y., Nelson, 1938, 456 p.

Timbres, H. G. & Timbres, (Mrs.) R. S. (Janney). *We didn't ask Utopia; a Quaker family in Soviet Russia.*
N. Y., Prentice-Hall, 1939, 290 p.

Treatment of some common diseases, edited by T. R. Hill.
Edinburgh, Livingstone, 1939, 398 p.

Treves, (Sir) F. *Surgical applied anatomy.* 10. ed.
London, Cassell, 1939, 748 p.

Tumors of the hands and feet, edited by George T. Pack.
St. Louis, Mosby, 1939, 138 p.

Walker, K. M. & Strauss, E. B. *Sexual disorders in the male.*
London, Hamilton, 1939, 248 p.

Weeks, P. H. *The big house of mystery; a physician-psychiatrist looks at ten thousand crimes and criminals.*
Phil., Dorrance, [1938], 259 p.

Westmann, S. K. *Sport, physical training*

and womanhood.
London, Bailliere, 1939, 222 p.

Wiener, A. S. *Blood groups and blood transfusion.* 2. ed.
Springfield, Ill., Thomas, [1939], 306 p.

Wiggers, C. J. *Physiology in health and disease.* 3. ed.
Phil., Lea, [1939], 1144 p.

Wilder, L. *The Mayo Clinic.* Rev. ed.
N. Y., Harcourt, [1939], 102 p.

Wright, H. N. G. & Montag, M. *A textbook of materia medica, pharmacology and therapeutics [for nurses].*
Phil., Saunders, 1939, 566 p.

DEATHS OF FELLOWS

Lynch, John Burgess: 17 West 74 Street, New York City; born in New York City, May 2, 1861; died in New York City, December 2, 1939; graduated in medicine from New York University in 1886; elected a Fellow of the Academy, October 6, 1898.

Dr. Lynch was consulting surgeon to the St. Francis and Nyack Hospitals and surgeon to the Hermann Knapp Memorial Eye Hospital.

Rogers, John: 177 East 71 Street, New York City; born in New York City, February 19, 1866; died in New York City, November 19, 1939; received the degree of A.B. in 1887, and Ph.B. in 1888 from Yale University; graduated in medicine from the College of Physicians and Surgeons, Columbia University, in 1891; elected a Fellow of the Academy December 7, 1905 and served as a member of the Committee on Admissions from January 1910 to January 1915.

Dr. Rogers was emeritus professor of clinical surgery at Cornell University Medical College and consulting surgeon to the Booth Memorial, Bellevue, New York Infirmary for Women and Children, St. Francis, Ruptured and Crippled and Memorial Hospitals, and the Stamford Hospital in Connecticut. He was a Fellow of the American College of Surgeons and the American Medical Association, and a member of the New York Surgical Society and the County and State Medical Societies.